The Sipholanes: A Novel Group of Triterpenes from the Marine Sponge *Siphonochalina siphonella*

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Eight new squalene-derived triterpenes possessing a hitherto unknown framework have been isolated from the Red Sea sponge *Siphonochalina siphonella*. The novel skeleton, designated sipholane, consists of a *cis*-octahydroazulene linked via an ethylene bridge to a *trans*-decahydrobenzoxepine. The structure of the sipholane skeleton was established by an X-ray diffraction analysis of one of the natural compounds derivatives (**16**). The structure of the latter made possible the NMR and mass spectral interpretations and, hence, the structure elucidation of the additional seven new compounds. The structural determinations were also assisted by various chemical correlations as well as transformations to compounds with well-defined functionalities. Of special interest is the suggested biogenesis of the sipholanes starting from 2,3:6,7:18,19-triepoxysqualene. In contrast to the single cyclization process that takes place in the biosynthesis of tetra- and pentacyclic triterpenes, the suggested route leading to the sipholanes involves two consecutive cyclizations.

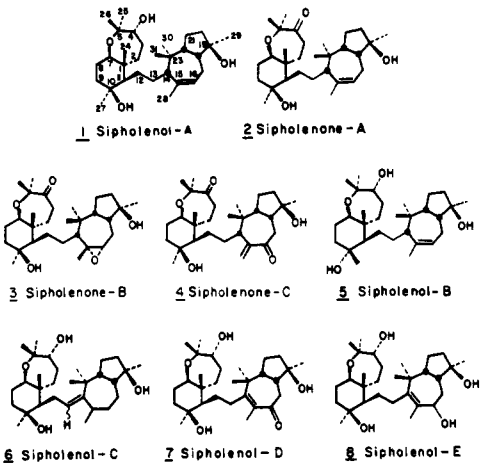
The terpenoids are to date the most abundant non-steroidal secondary metabolites isolated from marine sponges. Many interesting sesqui- di-, and sesterterpenes have been characterized from these animals.[1,2] However, to the best of our knowledge, until the isolation of the sipholanes,[3] aside from squalene, no other triterpenes have been reported. Most recently two additional triterpenes, possessing the terrestrial known malabricane skeleton, have been isolated from two sponges.[4,5]

The sipholanes possessing two separate uncommon bicyclic systems, linked to each other by an ethylene bridge, are unique among the triterpenes.

The structure of 8 out of the 11 pure triterpenes isolated from the petroleum ether exact of the Red Sea sponge *Siphonochalina siphonella* are reported herewith. Of the eight, sipholenol-A (**1**) and sipholenone-A (**2**) are the major components (ca. 1.8% and 0.75% dry weight of the animal, respectively). Three additional ones, sipholenone-B (**3**), sipholenol-B (**5**) and sipholenol-C (**6**) appear in somewhat smaller amounts, (ca. 0.07–0.16% dry weight) while the rest, compounds **4**, **7**, and **8**, exist in trace amounts only (ca. 0.01–0.03% dry weight).

The structure of the major triterpene isolated from the sponge, sipholenol-A (**1**), $C_{30}H_{52}O_4$, was established by an X-ray diffraction analysis of its monoacetate **16**[3,6] (Chart I).

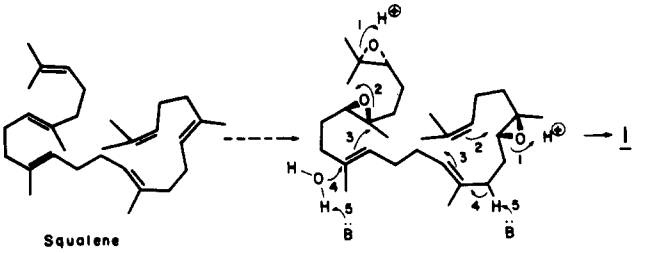
Chart I



Sipholenol-A (derived from squalene (Scheme I)) contains a *trans*-decahydrobenzoxepine and a *cis*-octahydroazulene moiety linked to each other by an ethylene bridge.

The structural information from the NMR spectra of compound **1** (as well as the other sipholanes, Tables I and II) is quite limited because of the relatively high number of unfunctionalized methylene groups and tertiary functional groups. Nevertheless, information on the molecule's

Scheme I. Suggested Biogenesis of the Sipholanes



conformation on the one hand and on the functional sites on the other hand can be readily obtained. Thus, from the coupling constants of the signals of H-4 and H-7 (Table I), the corresponding dihedral angles could be deduced ($\phi_{3\alpha,4\beta} \simeq 30°$, $\phi_{3\beta,4\beta} \simeq 90°$, $\phi_{8\beta,7\alpha} \simeq 170°$, and $\phi_{8\alpha,7\alpha} \simeq 60°$), suggesting a pseudoequatorial H-4 and an axial H-7. This geometry proposes, for the decahydrobenzoxepine moiety, a conformation in solution which is similar to the one found in the solid state.

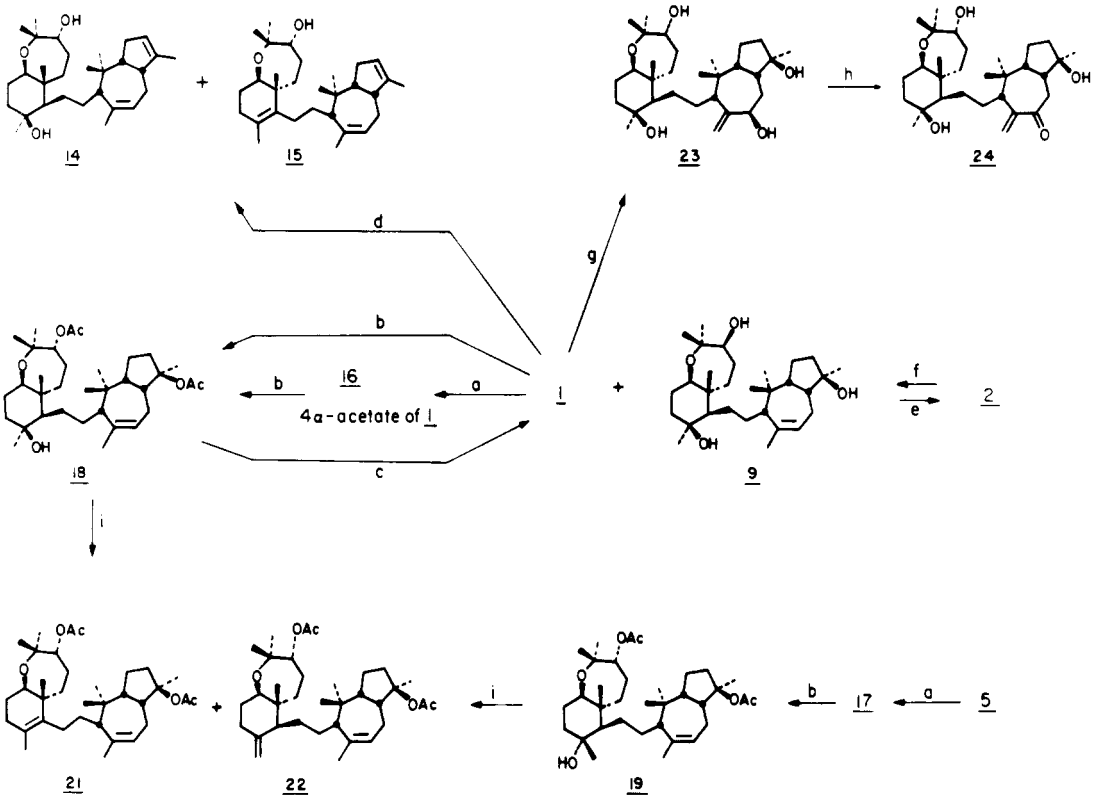
Comparisons of the ^{13}C NMR chemical shifts of the functional sites as well as other characteristic carbon atoms (Table II) are most useful in the structure determination of the new sipholanes reported hereafter.

Also of special value in the structure elucidation of the new compounds are the mass spectra (Table III). Three major fragmentations characterize these compounds: (1) cleavages of the perhydrobenzoxepine ring system (a and b); (2) several cleavages of the ethylene bridge (c–e), fragmentations that in part also involve one or more hy-

(1) Scheuer, P. J., Ed. "Marine Natural Products"; Academic Press: New York, 1978–1981; Vol. I–IV.
(2) Minale, L. In "Marine Natural Products"; Scheuer, P. J., Ed.; Academic Press: New York, 1978; Vol. I, p 175.
(3) Shmueli, U.; Carmely, S.; Groweiss, A.; Kashman, Y. *Tetrahedron Lett.* **1981**, *22*, 709.
(4) (a) Ravi, B. N.; Wells, R. T.; Croft, K. D. *J. Org. Chem.* **1982**, *46*, 1998. (b) McCabe, T.; Clardy, J.; Minale, L.; Pizza, C.; Zollo, F.; Riccio, R. *Tetrahedron Lett.* **1982**, *23*, 3307.
(5) Patou, W. F.; Paul, I. C.; Bajaj, A. G.; Dev, S. *Tetrahedron Lett.* **1979**, 4153.
(6) The IUPAC name of **16** is decahydro-2,2,5a,7-tetramethyl-6-[2-(1,2,3,3a,4,5,8,8a-octahydro-1-hydroxy-1,4,4,6-tetramethyl-5-azulenyl)-ethyl-1-benzoxepin-3,7-diol-3-acetate, and our name 4α-acetoxy-15-sipholen-10β,19β-diol. In order to simplify the discussions throughout this report, we have adopted a drawing of the formula in which the benzoxepine system is always at the left side and Me(24), H-22, and H-18 point up out of the plane (β-oriented, see Chart I).

0022-3263/83/1948-3517$01.50/0

Scheme II[a]



[a] (a) Ac_2O/pyridine, rt, overnight; (b) Ac_2O/pyridine, rt, 10 days. (c) 1% KOH/MeOH, (d) 3% *p*-TsOH/$CHCl_3$, 15 days; (e) Jones oxidation; (f) $NaBH_4$; (g) *m*-CPBA, $CHCl_3$; 0.5% *p*-TsOH/$CHCl_3$; (h) DDQ; (i) $SOCl_2$/Pyr, rt.

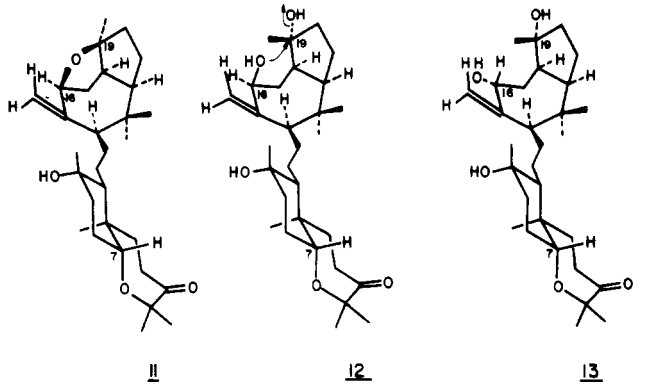


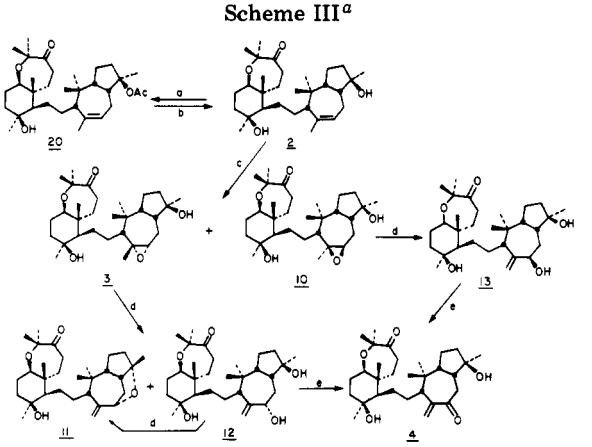
Figure 1.

drogen abstractions; and (3) cleavages of the octahydroazulene moiety (f–h) (see Table III). Because of the tertiary alcohol groups, it was not surprising to find that most fragments are accompanied by peaks resulting from loss of one–three molecules of water.

The structure of the second major compound, designated sipholenone-A (**2**), $C_{30}H_{50}O_4$, was suggested as the 4-keto derivative of **1** on the basis of its spectral data (ν_{max} 1705 cm^{-1}, δ 218.60 (C-4)). This hypothesis was confirmed by reduction of compound **2** to **1** (and to its 4-epimer **9**) as well as by Jones oxidation of **1** to give compound **2** (Scheme II). Comparison of the proton NMR spectra of **1** and **2** revealed in the spectrum of **2** two downfield protons suggested to be α to the CO group (δ 3.19 and 2.10). Outstanding also was the upfield shift of H-7 ($\Delta\delta$ = 0.56 ppm), best explained by the shielding cone of the carbonyl (Figure 1).

The third compound that was isolated from the sponge extract, sipholenone-B (**3**), $C_{30}H_{50}O_5$, was found to be closely related to compound **2**. According to the NMR

Scheme III[a]



[a] (a) Ac_2O/pyridine, rt, 10 days; (b) 1% KOH/MeOH; (c) *m*-CPBA, CH_2Cl_2; (d) 0.5% *p*-TsOH/$CHCl_3$; (e) Jones oxidation.

data (δ 2.90, t, J = 7.5 Hz, H-16 and δ 60.6 and 61.8 C-15 and C-16, respectively), compound **3** was proposed as the 15,16-epoxide of **2**. Indeed, epoxidation of **2** with *m*-chloroperbenzoic acid in CH_2Cl_2 at room temperature for 1.5 h gave two epimeric epoxides, **3** and **10** (Scheme III), of which the former was identical in all respects with the natural epoxide, sipholenone-B.[7] Because of the conformational flexibility of the cis bicyclic system and the cycloheptane ring, it was impossible to determine, on the basis of the NMR spectra alone, the stereochemistry of the two epimeric epoxides (**3** and **10**). The distinction between the two was achieved by their treatment with acid (Scheme III). Leaving compound **3** in $CHCl_3$ in the presence of

(7) Obtaining two epoxides was quite surprising because of steric hindrance, as can be observed from the Dreiding model.

Table I. ^{1}H NMR Chemical Shifts and Multiplicity Data (270 MHz, $CDCl_3$)

	compound											
	1			2			3			4		
H at C	δ	mult	J, Hz	δ	mult	J, Hz	δ	mult	J, Hz	δ	mult	J, Hz
3				3.19	ddd	13.0, 11.0, 2.4	3.22	ddd	13.0, 11.0, 2.5	3.23	ddd	13.0, 11.0, 2.5
				2.10	ddd	11.0, 6.3, 1.8	2.09	ddd	11.0, 6.3, 1.8	2.10	ddd	11.0, 6.3, 1.8
4	3.77	d	6.5									
7	3.46	dd	11.7, 4.4	2.90	dd	11.4, 3.8	2.92	dd	12.0, 4.3	2.92	dd	11.2, 4.0
16	5.39	br dd	8.2, 4.7	5.46	br dd	8.5, 4.8	2.90	t	7.5			
Me(24)	0.99	s		1.02	s		1.03	s		1.00	s	
Me(25)	1.24	s		1.31[a]	s		1.31[a]	s		1.31[a]	s	
Me(26)	1.13	s		1.26[a]	s		1.26[a]	s		1.27[a]	s	
Me(27)	1.25	s		1.25	s		1.28	s		1.34	s	
										6.15[b]	d	2.1
Me(28)	1.75	br s		1.76	br s		1.37	s				
										5.22[b]	d	1.8
Me(29)	1.09	s		1.15	s		1.17	s		1.14	s	
Me(30)	1.08	s		1.09	s		1.21	s		0.97	s	
Me(31)	1.03	s		1.09	s		1.27	s		1.12	s	

	compound											
	5			6			7			26 (8-Ac)		
H at C	δ	mult	J, Hz	δ	mult	J, Hz	δ	mult	J, Hz	δ	mult	J, Hz
4	3.82	d	6.4	3.79	d	6.5	3.83	d	6.5	4.96	d	6.9
7	3.60	dd	10.9, 5.0	3.64	dd	10.9, 4.4	3.54	dd	11.7, 4.8	3.55	dd	11.2, 4.3
13				5.34	t	7.0						
16	5.50	br dd	10.0, 4.5							4.28	dd	9.5, 6.6
Me(24)	0.82	s		0.96	s		0.98	s		1.05	s	
Me(25)	1.24	s		1.26	s		1.25	s		1.19	s	
Me(26)	1.12	s		1.11	s		1.13	s		1.14	s	
Me(27)	1.27	s		1.21	s		1.22	s		1.25	s	
Me(28)	1.77	br s		1.13	d	7.2	1.89	s		1.53	br s	
Me(29)	1.15	s		1.20	s		1.18	s		1.31	s	
Me(30)	1.09	s		0.88	s		0.75[a]	s		1.07	s	
Me(31)	1.03	s		0.89	s		1.00[a]	s		1.17	s	
Me(Ac)										2.13	s	

[a] The assignment of these peaks may be interchanged. [b] Terminal methylene.

Table II. ^{13}C NMR Chemical Shift Data (75.46 MHz, $CDCl_3$, ppm)

		compound							
C	mult	1	2	3	4	5	6	25	26
1	s	42.78	42.09	42.24	42.16	42.76	42.90	43.08	42.84
4	d/s	77.14	218.60	218.30	218.10	77.08	77.05	79.15	79.27
5	s	77.83	82.44	82.47	82.50	77.92	77.95	77.26	77.29
7	d	76.54	81.24	81.45	81.19	76.49	76.48	76.61	76.87
9	t	39.24	39.18	39.21	39.25	40.42	40.80	39.51	39.45
10	s	72.44	72.23	72.05	72.04	74.02	72.56	72.70	72.56
11	d	55.87	55.69	55.87	55.13	58.36	58.37	56.08	55.99
13	d						133.76		
14	d/s	57.73	57.70	56.23	57.02	57.71	140.05	161.98	163.51
15	s/d	143.23	143.02	60.63	147.56	143.69	33.85	132.74	120.36
16	d/s	121.37	121.57	61.86	202.57	121.73		199.75	71.93
18	d	52.87	52.78	53.23	51.29	52.84	50.84[a]	45.72[a]	58.75
19	s	82.14	81.99	81.75	82.38	82.28	73.58	71.33	70.49
22	d	48.95	48.80	47.36	48.91	48.94	50.12[a]	45.48[a]	55.99
23	s	35.50	35.50	37.18	37.08	35.55	33.35	35.59	31.55
24	q	13.03	12.22	12.19	12.23	12.94	13.15	13.09	13.30
28	t/q				125.83			11.71	19.23

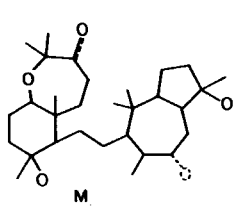
[a] The assignment of these peaks may be interchanged.

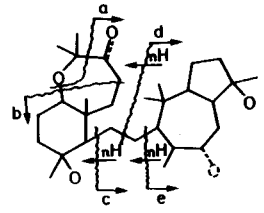
0.5% pTsOH for 24 h at room temperature gave two products: one (11) less polar and the other (12) more polar than the starting material. Prolonging the reaction time or treating pure compound 12 with acid, under the same conditions, afforded more of compound 11. Epoxide 10 under the same conditions gave a single compound (13).

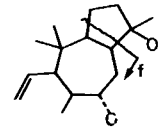
The acidic transformation of the latter epoxide (10 to 13), induced by the acidity of the $CDCl_3$, could be monitored in a NMR tube. The ^{1}H and ^{13}C NMR spectra clearly indicate that compounds 12 and 13 are the two 15(28)-en-16-ol epimers (see Experimental Section for the spectral data). Both epimers (12 and 13) gave upon oxidation with Jones reagent the same α,β-unsaturated ketone 4 (15(28)-en-16-one). Compound 11 under the same oxidative conditions remained unchanged.

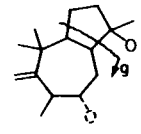
Obtaining ketone 4, from 12 and 13, provided the structure of the fourth isolated natural product, siphelenone-C, being identical in all respects with this ketone.

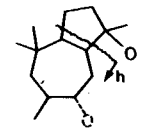
Table III. High-Resolution Mass Spectral Data











fragment	compound 1	2	5	23	24	25	26
M^+	476.3893 (1)					532.3721 (2)	533.3877 (2)[d]
$M^+ - H_2O$	458.3643 (11)	456.3613 (13)	458.3804 (3)	474.3643 (3)	472.3457 (10)	514.3599 (7)	516.3780 (3)
							515.3724 (14)[d]
$M^+ - 2H_2O$		438.3490 (4)	440.3622 (6)	456.3627 (12)	454.3421 (13)	496.3464 (4)	457.3593 (3)[d]
a[a] $- H_2O$	400.3319 (3)	398.3221 (2)					
a $- 2H_2O$	382.3238 (3)	380.3055 (2)	382.3214 (1)	398.3239 (12)			
b[a] $- H_2O$	356.3058 (5)		356.3066 (3)	372.2955 (7)	370.2852 (8)	370.2891 (2)	371.2926 (18)[d]
b $- 2H_2O$	338.2987 (3)		338.3031 (2)	355.2910 (14)[c]	353.2889 (29)[c]		
b $- H_2O - CH_3$	341.2860 (2)	341.2802 (3)	341.2827 (2)		355.2704 (17)		
c ($n = 1$)	234.1950 (16)	234.1965 (13)	234.1980 (5)	250.1886 (7)	248.1774 (28)	248.1776 (15)	250.1890 (20)
c ($n = 2$)[e]			233.1864 (1)	249.1810 (14)	247.1715 (32)	247.1717 (12)	249.1860 (86)
c $- H_2O$ ($n = 1$)		216.1878 (8)	216.1874 (13)	232.1822 (23)	230.1654 (30)	230.1651 (20)	
c $- H_2O$ ($n = 2$)[e]		215.1799 (3)	215.1799 (4)	231.1764 (19)	229.1639 (34)	229.1640 (22)	231.1721 (44)
d ($n = 1$)		220.1830 (2)	220.1827 (11)	236.1772 (10)	234.1586 (3)	234.1586 (11)	
d ($n = 2$)[e]	219.1736 (4)	219.1745 (1)	219.1746 (5)	235.1669 (12)	233.1526 (23)	233.1529 (30)	235.1647 (16)
d $- H_2O$ ($n = 1$)	202.1686 (4)	202.1707 (4)	202.1708 (10)	218.1727 (16)	216.1494 (20)	216.1496 (15)	
d $- H_2O$ ($n = 2$)[e]	201.1599 (8)	201.1638 (4)	201.1636 (12)		215.1471 (24)	215.1474 (20)	
d $- 2H_2O$ ($n = 1$)				200.1537 (15)			200.1605 (17)
d $- 2H_2O$ ($n = 2$)[e]				199.1482 (25)			
e ($n = 1$)			206.1649 (6)		222.1570 (8)		
e ($n = 2$)[e]			205.1582 (13)	223.1681 (45)	221.1519 (7)	221.1560 (6)	223.1644 (19)
e $- H_2O$ ($n = 1$)			188.1548 (4)	206.1703 (12)	204.1487 (30)		
e $- H_2O$ ($n = 2$)[e]			187.1482 (9)	205.1569 (38)	203.1417 (100)		205.1587 (35)
f[b]	163.1470 (2)		162.1390 (14)				178.1339 (14)
	162.1434 (5)	162.1394 (6)	161.1323 (27)				177.1261 (20)
g[b]		148.1255 (14)	148.1241 (34)			162.1046 (6)	164.1102 (15)
	147.1124 (19)		147.1167 (40)				
h[b]			134.1071 (25)				
		135.1164 (17)	133.1006 (38)			149.0947 (11)	

[a] For similar fragmentations, see ref 9. [b] For similar fragmentations in ring D of the steroidal skeleton, see ref 10. [c] b $- H_2O - OH$. [d] $M^+ - H$ and related fragments. [e] It cannot be excluded that this fragment results from fragmentation of the oxepine moiety.

The key compound for determining the stereochemistry of the epoxides **3** and **10** was compound **11**. As mentioned above, compound **11** is obtained via triol **12**. Dreiding models of the two 16-OH epimers (Figure 1) show clearly the proximity, due to the cis ring juncture, of a 16α-alcohol group to C-19. We believe this spatial closeness to be responsible for the facile 19-OH elimination in **12** and for the subsequent formation of the ethereal bridge from C-16 to C-19. Compound **12** is, therefore, the 16α-alcohol and **13** the 16β isomer. As no 16-OH epimerization takes place under the mild acidic conditions (as monitored by NMR), compound **13** is prevented geometrically from forming an oxygen bridge (Figure 1). For this reason, the 19-OH elimination also does not take place. Obviously the above results also determine the stereochemistry of the epoxides, i.e., compound **3** is the α-epoxide and **10** the β-isomer. Under stronger acidic conditions, water elimination occurred (Scheme II). Thus, compound **1** afforded, after 15–20 days in 3% *p*-TsOH/$CHCl_3$, the diene **14** and the triene **15** (again the 19-OH group was the first one to be eliminated). Refluxing of the acidic reaction mixture in order to facilitate the elimination resulted in decomposition. Noteworthy is the ^{13}C NMR resonance line of C-16 in compound **11**, which is strongly shifted downfield (13 ppm!) following the cyclization process.

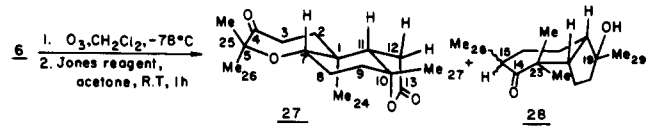
Another triol that was isolated from the petroleum ether extract of the sponge was sipholenol-B (**5**), $C_{30}H_{52}O_4$. The only changes in the ^{13}C NMR chemical shifts of C-9 (δ 40.4 in **5** and 39.2 in **1**), C-10, and C-11 (see Table II), together with the change in the proton NMR of Me-24 (δ 0.82 in **5** and 0.99 in **1**), suggest compound **5** to be the 10-epimer of **1**. We have therefore decided on a 10-OH elimination in comparing compounds **1** and **5**.

In order to avoid the elimination of the other two alcohol groups, their protection was required. As expected, overnight acetylation (pyridine/Ac_2O) gave the 4-acetate. Fortunately, after 7–10 days the 19-hydroxyl was also esterified, whereas the 10-OH remained intact.[8] From comparisons of the acetylation rates of various sipholanes (Ac_2O/pyridine, room temperature), it is apparent that a double bond or a α-oriented oxygen at the 15(16)-position enhances the esterification. Thus, e.g., compounds **2** and **3** afford after 10 days the 19-acetates (**20** and **3a**, respectively).

Both 10-hydroxy 4,19-diacetates (**18** and **19**, see Scheme II) were submitted to $SOCl_2$/pyridine elimination. Compound **18** in which the 10-OH group is axial afforded a single olefin, **21**, while compound **19** with the equatorial 10-hydroxyl gave two compounds in a ratio of 1:1. Of the two, the less polar one was identical in all respects with compound **21**, obtained from **18**, proving thereby that sipholenol-B (**5**) is indeed the 10-epimer of **1** (Scheme II). The ^1H and ^{13}C NMR spectral data (Tables I and II) clearly indicate that compound **21**, possessing a tetrasubstituted double bond, is the $\Delta^{10(11)}$-olefin while **22**, the second compound obtained from **19**, with an exocyclic double bond, is the $\Delta^{10(27)}$-isomer. The fact that a single olefin is obtained from **18** and two isomers are obtained from **19** is in full agreement with their 10-axial and 10-equatorial hydroxyls, respectively.

Compound **6**, $C_{30}H_{52}O_4$, designated sipholenol-C was also found to be a triol; however, it was not as closely related to compound **1** as the previously discussed triol **5**. The NMR and mass spectra of **6** pointed clearly to the existence of the decahydrobenzoxepine moiety as in **1**, (Tables I and II) as well as changes in the rest of the molecule. The four Me groups of the decahydroazulene moiety still exist in **6**; however, one of them (Me-28, a singlet in **2** and **5**) changes place and multiplicity, i.e., it gives rise to a doublet at δ 1.13 (J = 7.2 Hz) (the methine hydrogen resonating at δ 1.90). In the absence of the vinylic methyl the >$CHCH_2CH$=C< moiety (δ 2.27, dd (J = 6.0 and 7.0 Hz, 2 H) and 5.34, t (J = 7.0 Hz)) has to be in a different position. On the basis of the above and additional spectral data (e.g., the chemical shifts of the C atoms of the oxepine moiety that are, except for C-11 which is influenced by the C-13 double bond, identical with the δ values of **1**), sipholenol-C is assigned as the Δ^{13}-isomer of **1**.

Scheme IV



^1H NMR data of compound **27**

H at C[a]	δ	mult	J, Hz
2a	1.61	m	
2e	1.65	m	
3a	3.19	ddd	3.0, 11.6, 13.7
3e	2.21	ddd	2.6, 6.4, 11.6
7	3.00	dd	4.7, 10.7
8a	1.72	m	
8e	1.82	m	
9a	1.74	m	
9e	2.02	ddd	2.6, 4.0, 11.2
11	1.81	dd	6.4, 14.6
12a	2.49	dd	14.6, 16.3
12e	2.30	dd	6.4, 16.3
24	1.07	s	
25	1.32	s	
26	1.27	s	
27	1.39	s	

[a] a = axial proton; e = equatorial proton.

Unequivocal proof of the structure was obtained by ozonolysis of **6**, which split the molecule into two parts (Scheme IV). Jones oxidation of the ozonide gave two products; a γ-lactone (**27**), obtained by oxidation of the initially formed γ-lactol (closure of 13-CHO to 10-OH), and a hydroxyketone (**28**). Of the two, the spectra of compound **27** was most informative—see Scheme IV, and its structure confirmed the position of the double bond in **6**.

Of the three compounds that were isolated from the sponge in trace amounts (**4**, **7**, and **8**) two, compounds **7** and **8**, are closely related. Both **7**, $C_{30}H_{50}O_5$, and **8**, $C_{30}H_{52}O_5$, incorporate in their structure the characteristic sipholane decahydrobenzoxepine moiety (see Tables I–III for the NMR and mass spectra). Both **7** and **8** were purified as the 4-monoacetates, **25** and **26**, respectively (compound **7** was also obtained in small amounts as the free alcohol). The NMR spectra of **25** shows clearly the benzoxepine grouping, as in compound **1**, as well as the *gem*-dimethyl and methylcarbinol of the octahydroazulene system. In addition, the latter moiety also possesses an α,β-unsaturated tetrasubstituted ketone (ν_{max} 1660 cm^{-1}; δ_c 199.7 s (C-16), 132.7 s (C-15), 162.0 s (C-14) and δ_H 1.90 s (3H, =$C(CH_3)CO$). An ABX system assigned to the methylene α to the ketone (δ 2.37 and 2.31) expands further the carbonyl moiety to >C=$C(CH_3)COCH_2CH$ < and suggests for **7** the 14-en-16-one structure.

Compound **8**, sipholenol-E, was proposed to be the 14-en-16-alcohol. The ^{13}C NMR of this compound (Table II) exhibits a tetrasubstituted double bond bearing a vinyl

(8) Hikino, H.; Konno, C.; Takemoto, T. *Chem. Pharm. Bull. Jpn.* **1971**, *19*, 93.
(9) McLafferty, F. W. "Interpretation of Mass Spectra"; Turro, N. J., Ed.; University Science Books: California, 1980; pp 189–215.
(10) Zaretskii, Z. V. "Mass Spectrometry of Steroids"; Keter Publishing House: Jerusalem, 1976.

methyl (δ_H 1.54). Furthermore, the relative low field of the CHOH signal (δ 4.28 dd, J = 9.5 and 6.6 Hz) is in accordance with its allylic position.

Finally, Jones oxidation of sipholenol-E (**8**) afforded compound **7**, confirming thereby the structural relationship of the two compounds. In full agreement with the structure are the mass spectrum fragmentation patterns of **25** and **26** (the 4-monoacetates of compounds **7** and **8**, respectively), which were compared with the fragmentations of compounds **23** and **24**. The latter pair, 15(28)-en-16-ol (**23**) and 15(28)-en-16-one (**24**), were prepared especially from compound **1** (see Scheme II) for the mass spectrum fragmentation comparison (see Table III, e.g., fragments c–h).

Of interest is the biogenesis of the new triterpenes starting from squalene (Scheme I). The isolation of a 10-ol epimeric pair (**1** and **5**) is in accordance with the suggested mechanism, i.e., the H_2O quenching being the last step of the cyclization process. A similar oxidation of the nonterminal double bond of squalene followed by the formation of an ethereal bridge is suggested in the biogenesis of malabaricanol.[5]

The suggested biogenesis calls for two cyclization initiations. In this context it was interesting to isolate, from the crude extract of the sponge, another triterpene which lacks the octahydroazulene moiety—the structure of this compound will be the subject of a forthcoming report.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Model 177 spectrophotometer. Optical rotations were measured on a Perkin-Elmer Model 141 polarimeter using a 10-cm microcel. ^{1}H NMR spectra were recorded on a Bruker WH-270 or Bruker WH-300 NMR spectrometer, and ^{13}C NMR spectra were recorded on a Bruker WH-90 (22.63 MHz) or Bruker WH-300 (75.46 MHz) NMR spectrometer; all chemical shifts are reported with respect to Me_4Si (δ = 0). Low-resolution mass spectra were recorded on a Du Pont 21-491B mass spectrometer. High-resolution mass spectra were recorded on a Varian MAT 731 mass spectrometer. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are reported uncorrected. All solvents used were either spectral grade or freshly distilled.

Isolation of Sipholanes 1–8 from *Siphonochalina siphonella*. The sponge *Siphonochalina siphonella* (Levi, 1965) was collected near Naâma in the Gulf of Eliat in July, 1979. The sponge was deep-frozen immediately after collection and then freeze-dried to give the dry material (210 g). Dry sponge (150 g) was extracted with petroleum ether in a Soxhlet apparatus for 10 h. Evaporation of the solvent gave a brown gum (13.3 g, 8.9% dry weight).

The crude extract (13.3 g) was applied to a column of silica gel H (150 g), and the material was eluted with solvent of gradually increasing polarity, from $CHCl_3$ through EtOAc.

Fractions 2–4 (100 mL each), eluted with $CHCl_3$, contained a mixture of compound **1**, compound **2**, and a mixture of sterols (6.2 g). The combined fractions 2–4 were rechromatographed on a column of Sephadex LH-20 with $CHCl_3$/petroleum ether (65:35) as eluant to yield in fractions 6–9 (50 mL each), a mixture of compound **2** and sterols (3.5 g). Fractions 11–15 yielded pure compound **1** (2.7 g, 1.8% dry weight). Fractions 6–9 (3.5 g) were flash chromatographed again on a silica gel H column (70 g silica), eluted with $CHCl_3$/petroleum ether (40:60) to afford in fractions 2–15 (50 mL each) a mixture of sterols (1.9 g) and in fractions 18–32 pure compound **2** (1.12 g, 0.75% dry weight).

Fractions 6 and 7 from the first chromatography, eluted with 10% EtOAc in $CHCl_3$ gave compound **3** (102 mg, 0.07% dry weight) and compound **4** (35 mg, 0.02% dry weight), respectively. Fractions 8–10, eluted with 30% EtOAc in $CHCl_3$, yielded compound **5** (240 mg, 0.16% dry weight). Fractions 11–13, eluted with EtOAc/$CHCl_3$ (1:1), gave compound **6** (150 mg, 0.1% dry weight). Fraction 14, eluted with pure EtOAc yielded compound **7** (6 mg). Fraction 15, eluted with EtOAc, gave a mixture of compounds **7** and **8** (57 mg). Separation of the two was achieved upon acetylation (Ac_2O/pyridine, room temperature) followed by evaporation of the solvent mixture and then chromatography on a silica gel H (2 g) column eluted with solvent of gradually increasing polarity. Fractions 8–11, eluted with 5% EtOAc in $CHCl_3$ (5 mL each), contained compound **25** (35 mg, 0.03% dry weight). Fractions 13–17, eluted with 10–20% EtOAc in $CHCl_3$ gave compound **26** (15 mg, 0.01% dry weight).

Sipholenol-A (1): mp 169–171 °C (acetone/petroleum ether); $[\alpha]^{24}_D$ –60° (c 7.2, $CHCl_3$); IR (KBr) 3430, 2970, 1470, 1440, 1375, 1165, 1125, 1080, 1060, 1050, 910, 765 cm^{-1}; ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 143.23 (s), 121.37 (d), 82.14 (s), 77.83 (s), 77.17 (d), 76.54 (d), 72.44 (s), 57.73 (d), 55.87 (d), 52.87 (d), 48.95 (d), 42.78 (d), 39.24 (t), 37.27 (t), 35.50 (s), 34.02 (t), 33.82 (t), 31.70 (q), 30.14 (q), 29.90 (t), 29.51 (q), 29.18 (q), 26.93 (t), 26.72 (t), 25.83 (q), 25.28 (q), 25.04 (t), 24.83 (t), 21.42 (q), 13.03 (q). For ^{1}H NMR and mass spectral data, see Tables I and III, respectively.

Sipholenone-A (2): mp 187–188 °C (acetone/petroleum ether); $[\alpha]^{24}_D$ –29° (c 9.0, $CHCl_3$); IR (KBr) 3450, 2950, 1705, 1465, 1370, 1170, 1130, 1080, 1045, 910 cm^{-1}; ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 218.06 (s), 143.02 (s), 121.57 (d), 82.44 (s), 81.99 (s), 81.24 (d), 72.23 (s), 57.70 (d), 55.69 (d), 52.78 (d), 48.80 (d), 42.09 (s), 39.69 (t), 39.18 (t), 37.33 (t), 35.50 (s), 35.02 (q), 33.82 (t), 31.67 (q), 30.08 (q), 30.05 (q), 29.45 (q), 26.90 (t), 26.69 (t), 26.54 (t), 25.55 (q), 25.04 (t), 24.80 (t), 20.45 (q), 12.22 (q). For ^{1}H NMR and mass spectral data, see Tables I and III, respectively.

Sipholenone-B (3): an oil; $[\alpha]^{24}_D$ +5° (c 4.4, $CHCl_3$); IR ($CHCl_3$) 3450, 2940, 2875, 1700, 1455, 1435, 1370, 1285, 1240, 1165, 1120, 1065, 1035, 910, 875 cm^{-1}; ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 218.30 (s), 82.47 (s), 81.75 (s), 81.45 (d), 72.05 (s), 61.86 (d), 60.63 (s), 56.23 (d), 55.87 (d), 53.23 (d), 47.36 (d), 42.24 (s), 39.84 (t), 39.21 (t), 37.48 (t), 37.18 (s), 35.14 (q), 33.58 (t), 33.34 (q), 30.68 (q), 30.47 (q), 29.99 (q), 28.43 (t), 27.86 (t), 26.72 (t), 26.69 (t), 25.73 (q), 24.03 (t), 20.52 (q), 12.19 (q); mass spectrum (EI, 12 eV) m/e (relative intensity) 472 ($M^+ - H_2O$, 6), 454 (7), 436 (4), 373 (10), 355 (6), 329 (8), 303 (5), 249 (6), 245 (5), 236 (6), 205 (66), 150 (53), 123 (35), 83 (100). For ^{1}H NMR data, see Table I.

Sipholenone-C (4): an oil; $[\alpha]^{24}_D$ +1° (c 0.9, $CHCl_3$); IR ($CHCl_3$) 3590, 3450, 2920, 2860, 1705, 1675, 1595, 1372, 1250, 1160, 1070, 1035, 905 cm^{-1}; ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 218.10 (s), 202.57 (s), 147.56 (s), 125.83 (t), 82.50 (s), 82.38 (s), 81.19 (d), 72.04 (s), 57.02 (d), 55.13 (d), 51.29 (d), 48.91 (d), 42.29 (t), 42.16 (s), 39.94 (t), 39.25 (t), 37.11 (t), 37.08 (s), 35.06 (q), 33.87 (t), 33.01 (q), 30.31 (q), 28.48 (q), 26.69 (q), 26.54 (t), 26.41 (t), 25.86 (t), 24.85 (t), 20.50 (q), 12.23 (q); mass spectrum (CI, isobutane), m/e (relative intensity) 489 (MH^+, 12), 471 ($MH^+ - H_2O$, 85), 453 ($MH^+ - 2H_2O$, 100). For ^{1}H NMR spectral data, see Table I.

Sipholenol-B (5): an oil; $[\alpha]^{24}_D$ –37° (c 5.2, $CHCl_3$); IR ($CHCl_3$) 3460, 2920, 2870, 1460, 1380, 1260, 1200, 1180, 1150, 1070, 1000, 910, 865 cm^{-1}; ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 143.70 (s), 121.73 (d), 82.25 (s), 77.95 (s), 77.14 (d), 76.51 (d), 74.03(s), 58.44 (d), 57.79 (d), 52.90 (d), 48.96 (d), 42.89 (s), 40.42 (t), 37.36 (t), 35.56 (s), 34.73 (t), 33.54 (t), 31.47 (q), 30.08 (q), 29.52 (q), 29.07 (q), 28.94 (t), 27.05 (t), 25.61 (q), 25.48 (t), 25.10 (t), 24.82 (t), 23.63 (q), 21.56 (q), 12.97 (q). For ^{1}H NMR and mass spectral data, see Tables I and III.

Sipholenol-C (6): an oil; $[\alpha]^{24}_D$ –28° (c 1.7, $CHCl_3$); IR ($CHCl_3$) 3430, 2930, 2860, 1450, 1375, 1160, 1135, 1080, 1000, 905, 860 cm^{-1}; ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 140.05 (s), 133.76 (d), 77.95 (s), 77.05 (d), 76.48 (d), 73.58 (s), 72.56 (s), 58.37 (d), 50.84 (d), 50.12 (d), 42.90 (s), 40.80 (t), 37.24 (t), 35.23 (t), 33.85 (d), 33.55 (t), 33.35 (s), 32.17 (t), 29.93 (q), 29.06 (q), 28.85 (q), 28.76 (t), 26.30 (q), 25.64 (t), 24.00 (t), 23.49 (q), 22.35 (q), 21.51 (q), 21.41 (t), 13.15 (q); high-resolution mass spectrum (EI, 70 eV), m/e (relative intensity) 440.3740 ($C_{30}H_{48}O_2$, $M^+ - 2H_2O$, 14.6), 231.1735 ($C_{16}H_{23}O$, 10), 214.1738 ($C_{16}H_{22}$, 9.2). For ^{1}H NMR data, see Table I.

Sipholenol-D (7): an oil; $[\alpha]^{24}_D$ –31° (c 0.2, $CHCl_3$); IR ($CHCl_3$) 3590, 3450, 2920, 2870, 1660, 1645, 1440, 1360, 1245, 1070, 1032, 960, 905 cm^{-1}. For ^{1}H NMR data, see Table I.

Sipholenol-E monoacetate (26): an oil; $[\alpha]^{24}_D$ –12° (c 0.6, $CHCl_3$); IR ($CHCl_3$) 3580, 3440, 2920, 2870, 1720, 1440, 1360, 1245, 1075, 1035, 960, 905, 885 cm^{-1}; ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 170.25 (s), 163.51 (s), 120.36 (s), 79.27 (d), 77.29 (s), 76.87 (d), 72.56 (s), 71.93 (d), 70.49 (s), 58.75 (d), 55.99 (d, ×2), 42.84 (s), 40.26 (t), 40.11 (t), 39.45 (t), 37.93 (t), 36.10 (t), 35.77 (t), 35.59 (q), 32.77

(q), 31.55 (s), 30.38 (q, ×2), 29.09 (t), 26.63 (q), 25.52 (t), 23.07 (t), 21.48 (q), 20.94 (q), 19.23 (q), 13.30 (q). For ^{1}H NMR and mass spectral data, see Tables I and III, respectively.

Reduction of Compound 2 with Sodium Borohydride. $NaBH_4$ (200 mg) was added in portions to a solution of **2** (100 mg) in MeOH (10 mL), and the solution was stirred at 0 °C for 3 h. The excess of the reagent was destroyed with 10% aqueous AcOH (5 mL). The solvent was then evaporated and the residual water extracted with $CHCl_3$ (3 × 20 mL). The combined $CHCl_3$ phases were dried over anhydrous $MgSO_4$ and the solvent was evaporated. The residue (95 mg) was chromatographed on silica gel H with increasing percent of $CHCl_3$ in petroleum ether to yield the two isomeric alcohols **1** and **9**. Compound **1**, 40 mg (40% theoretical) was found to be identical in all respects with the natural product. Compound **9**: 26 mg (26% theoretical); an oil; IR ($CHCl_3$) 3600, 3440, 2940, 2860, 1440, 1370, 1075, 1030, 900 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.97 (3 H, s), 1.04 (3 H, s), 1.088 (3 H, s), 1.094 (3 H, s), 1.12 (3 H, s), 1.26 (3 H, s), 1.24 (3 H, s), 1.76 (3 H, br s), 3.16 (1 H, dd, J = 11.2, 3.8 Hz), 3.65 (1 H, d, J = 10.0 Hz), 5.47 (1 H br dd, J = 8.7, 4.8 Hz); mass spectrum (CI, isobutane), m/e (relative intensity) 477 (MH^+, 1), 459 ($MH^+ - H_2O$, 50), 441 (50), 399 (90), 381 (100).

Jones Oxidation of Compound 1. Jones oxidation of **1** (20 mg) in the same manner as described for **12** gave ketone **2** (19 mg, 95% theoretical), identical in all respects with the authentic sample.

Epoxidation of Compound 2 with *m*-Chloroperbenzoic Acid. To a cooled (0 °C) solution of **2** (118 mg) in CH_2Cl_2 (15 mL) was added a solution of *m*-chloroperbenzoic acid (70 mg) in CH_2Cl_2 (5 mL). The reaction mixture was kept at room temperature for 1.5 h, washed with aqueous $NaHCO_3$ and water, dried over anhydrous $MgSO_4$, and evaporated. The residue (130 mg) as chromatographed on silica gel H with $CHCl_3$ as eluant to afford the two isomer epoxides **3** and **10**. The less polar isomer, 39 mg (32% theoretical), was found to be identical with compound **3**.

More polar isomer **10**: 27 mg (22% theoretical); an oil; IR ($CHCl_3$) 3420, 2935, 2870, 1700, 1450, 1373, 1070, 1040, 905 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.90 (3 H, s), 1.01 (3 H, s), 1.17 (3 H, s), 1.20 (3 H, s), 1.26 (3 H, s), 1.31 (3 H, s), 1.37 (3 H, s), 1.39 (3 H, s), 2.56 (1 H, br q, J = 7.5 Hz), 2.74 (1 H, dd, J = 9.0, 5.5 Hz), 2.94 (1 H, dd, J = 12.0, 4.2 Hz), 3.22 (1 H, ddd, J = 12.9, 11.0, 2.5 Hz); mass spectrum (EI, 10 eV), m/e (relative intensity) 472 ($M^+ - H_2O$, 1), 454 (5), 444 (1), 436 (3), 426 (10), 422 (13), 205 (30), 85 (67), 83 (100); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 218.36 (s), 82.83 (s), 82.38 (s), 81.30 (d), 71.84 (s), 60.48 (d), 60.48 (s), 56.08 (d), 52.78 (d), 51.17 (d), 48.86 (d), 42.15 (s), 39.69 (t), 38.91 (t), 38.91 (t), 37.66 (s), 35.08 (q), 35.08 (t), 32.47 (q), 31.43 (t), 30.74 (t), 30.74 (t), 28.13 (t), 26.60 (q), 25.73 (t), 25.73 (q), 24.06 (q), 21.63 (q), 20.50 (q), 12.19 (q).

Treatment of 3 with *p*-Toluenesulfonic Acid. A solution of **3** (21 mg) and *p*-TsOH acid (0.1 mg) in $CHCl_3$ (10 mL) was kept for 18 h at room temperature. The $CHCl_3$ solution was then washed with aqueous $NaHCO_3$ solution and dried over anhydrous $MgSO_4$. The solvent was evaporated and the residue chromatographed on silica gel with increasing percent of EtOAc in $CHCl_3$. Less polar component **11**: 10 mg (49% theoretical), an oil; IR ($CHCl_3$) 3580, 3405, 2920, 2855, 1700, 1455, 1440, 1370, 1350, 1160, 995, 900 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.96 (3 H, s), 1.10 (3 H, s), 1.13 (3 H, s), 1.14 (3 H, s), 1.20 (3 H, s), 1.26 (3 H, s), 1.31 (3 H, s), 2.92 (1 H, dd, J = 11.9, 3.9 Hz), 3.21 (1 H, ddd, J = 13.5, 11.2, 2.5 Hz), 4.69 (1 H, d, J = 7.9 Hz), 4.74 (1 H, br s), 5.04 (1 H, br s); mass spectrum (EI, 12 eV), m/e (relative intensity) 472 (M^+, 4), 454 (8), 412 (8), 395 (21), 372 (20), 328 (14), 297 (14), 227 (23), 218 (25), 97 (100); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 218.16 (s), 151.46 (s), 113.31 (t), 94.23 (s), 82.68 (d), 82.45 (s), 81.39 (d), 72.29 (s), 55.25 (d), 52.20 (d), 51.11 (d), 42.16 (s), 39.81 (t), 39.13 (t), 36.73 (d), 36.73 (s), 35.13 (q) 35.13 (q), 32.66 (t), 32.40 (t), 30.79 (q), 29.73 (t), 29.12 (q), 28.13 (t), 26.74 (t), 26.62 (t), 26.36 (t), 25.02 (q), 20.52 (q), 12.18 (q).

Polar component **12**, 4 mg (19% theoretical), is also an oil; IR ($CHCl_3$) 3400, 2920, 2860, 1700, 1458, 1440, 1370, 1360, 1160, 1130, 1112, 1070, 1000, 990, 900 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.92 (3 H, s), 0.95 (3 H, s), 1.14 (3 H, s), 1.16 (3 H, s), 1.26 (3 H, s), 1.28 (3 H, s), 1.32 (3 H, s), 2.93 (1 H, dd, J = 11.9, 3.9 Hz), 3.22 (1 H, ddd, J = 13.6, 10.9, 2.0 Hz), 4.25 (1 H, dd, J = 10.5, 5.6 Hz), 4.90 (1 H, br s), 5.27 (1 H, br s); mass spectrum (CI, isobutane), m/e (relative intensity) 491, (MH^+, 27), 473 (100), 455 (87), 437 (20).

Treatment of 10 with *p*-Toluenesulfonic Acid. A solution of **10** (23 mg) and *p*-TsOH acid (0.1 mg) in $CHCl_3$ (10 mL) was kept for 18 h at room temperature. The $CHCl_3$ solution was then washed with aqueous $NaHCO_3$ solution and dried over anhydrous $MgSO_4$. The solvent was evaporated to yield a single product (**13**): 21 mg (91% theoretical); an oil; IR ($CHCl_3$) 3585, 3400, 2920, 1705, 1440, 1372, 1160, 1125, 1070, 1035, 910 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.82 (3 H, s), 0.96 (3 H, s), 1.10 (3 H, s), 1.14 (3 H, s), 1.23 (3 H, s), 1.26 (3 H, s), 1.31 (3 H, s), 2.92 (1 H, dd, J = 11.9, 4.3 Hz), 3.21 (1 H, ddd, J = 13.5, 10.9, 2.0 Hz), 4.43 (1 H, t, J = 4.6 Hz), 4.84 (1 H, br s), 5.22 (1 H, br s); mass spectrum (EI, 12 eV), m/e (relative intensity) 454 ($M^+ - 2H_2O$, 10), 436 (4), 397 (3), 341 (5), 256 (13), 223 (9), 205 (20), 184 (37), 156 (70), 149 (100); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 218.06 (s), 152.03 (s), 113.45 (t), 82.44 (s), 81.99 (s), 81.15 (d), 72.37 (s), 72.20 (d), 55.24 (d), 51.32 (d), 46.79 (d), 42.18 (s), 39.78 (t), 39.36 (d), 39.12 (t), 36.97 (s), 35.05 (q), 35.05 (q), 32.65 (t), 32.50 (q), 32.17 (t), 30.41 (q), 26.69 (t), 26.51 (t), 25.82 (t), 25.52 (t), 25.01 (q), 23.79 (t), 20.49 (q), 12.22 (q).

Jones Oxidation of Compound 12. Jones reagent (2 drops) was added to a stirred solution of **12** (10 mg) in acetone (2 mL). The reaction mixture was kept at 0 °C for 10 min, and the excess of the reagent was then destroyed by the addition of a few drops of MeOH. The reaction mixture was worked up as usual to yield ketone **4**: 9 mg (90% theoretical); an oil; IR ($CHCl_3$) 3590, 3450, 2920, 2860, 1705, 1675, 1595, 1460, 1372, 1250, 1160, 1070, 1035, 905 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.97 (3 H, s), 1.00 (3 H, s), 1.12 (3 H, s), 1.14 (3 H, s), 1.27 (3 H, s), 1.31 (3 H, s), 1.34 (3 H, s), 2.92 (1 H, dd, J = 11.2, 4.0 Hz), 3.23 (1 H, ddd, J = 13.5, 10.9, 2.1 Hz), 5.22 (1 H, d, J = 1.8 Hz), 6.15 (1 H, d, J = 2.1 Hz); mass spectrum (CI, isobutane), m/e (relative intensity) 489 (MH^+, 12), 471 (85), 453 (100).

Jones Oxidation of Compound 13. Jones oxidation of compound **13** (15 mg) in the same manner as described above for **12** gave the same α,β-unsaturated ketone **4** as obtained from **12** (14 mg, 94% theoretical).

Treatment of Alcohol 12 with *p*-Toluenesulfonic Acid. A solution of **12** (10 mg) and *p*-TsOH (0.1 mg) in $CHCl_3$ (5 mL) was kept for 72 h at room temperature. The $CHCl_3$ solution was worked up as described above to yield the ether **11** (9 mg, 91% theoretical).

Acid-Catalyzed Elimination of Sipholenol-A (2). Sipholenol-A (**2**, 200 mg) dissolved in $CHCl_3$ (15 mL) in the presence of *p*-TsOH acid (5 mg) was kept at room temperature for 17 days. The $CHCl_3$ was then removed under vacuum and the residue applied to a silica gel H column using increasing percent of EtOAc in petroleum ether as eluant. The less polar component (**14**) was eluted with 20% EtOAc in petroleum ether and the more polar one (**15**) with 30% EtOAc in petroleum ether.

Compound 14: an oil; IR ($CHCl_3$) 3600, 3400, 2900, 1445, 1380, 1210, 1085, 910 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.99 (3 H, s), 1.02 (3 H, s), 1.07 (3 H, s), 1.10 (3 H, s), 1.13 (3 H, s), 1.26 (3 H, s), 1.67 (3 H, br s), 1.76 (3 H, br s), 3.50 (1 H, dd, J = 11.7, 4.1 Hz), 3.81 (1 H, d, J = 6.8 Hz), 5.29 (1 H, br s), 5.50 (1 H, br dd, J = 9.0, 5.0 Hz); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 146.46 (s), 142.99 (s), 123.51 (d), 121.60 (d), 77.83 (s), 77.11 (d), 76.56 (d), 72.44 (s), 57.10 (d), 56.41 (d), 55.81 (d), 45.24 (d), 42.72 (s), 39.12 (t), 35.29 (s), 34.00 (q), 33.94 (t), 33.28 (q), 31.28 (q), 29.93 (t), 29.36 (q), 29.15 (t), 26.84 (t), 26.72 (t), 26.48 (t), 25.22 (t), 21.42 (q), 15.34 (q), 13.00 (q); mass spectrum (EI, 12 eV), m/e (relative intensity) 458 (M^+, 2), 440 (8), 400 (3), 382 (17), 337 (20), 294 (10), 222 (15), 214 (22), 200 (23), 188 (22), 146 (47), 133 (39), 122 (100).

Compound 15: an oil; IR ($CHCl_3$) 3600, 3400, 2900, 2850, 1440, 1370, 1200, 1090, 930 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.98 (3 H, s), 1.02 (3 H, s), 1.10 (3 H, s), 1.15 (3 H, s), 1.28 (3 H, s), 1.53 (3 H, s), 1.68 (3 H, br s), 1.76 (3 H, br s), 3.71 (1 H, dd, J = 12.0, 4.4 Hz), 3.81 (1 H, d, J = 6.5 Hz), 5.29 (1 H, br s), 5.50 (1 H, br dd, J = 9.0, 5.0 Hz); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 146.40 (s), 143.02 (s), 138.13 (s), 125.97 (s), 123.66 (d), 121.78 (d), 78.04 (s), 77.32 (d), 75.13 (d), 57.31 (d), 56.47 (d), 45.30 (d), 43.17 (s), 35.41 (s), 34.03 (t), 32.17 (t), 31.76 (t), 31.31 (q), 30.02 (t), 29.75 (t), 29.75 (q), 29.39 (q), 29.12 (q) 28.58 (t), 27.56 (t), 27.14 (t), 21.87 (q), 19.25 (q), 17.85 (q), 15.37 (q); mass spectrum (EI, 10 eV), m/e (relative intensity) 440 (M^+, 1), 410 (8), 372 (3), 340 (17), 255 (24),

214 (23), 170 (18), 147 (48), 134 (86), 128 (76), 81 (100).

Acetylation of Compound 1 with Acetic Anhydride in Pyridine. Acetylation of compound 1 (200 mg) with a 1:1 Ac_2O/pyridine solution (1 mL), at room temperature overnight, afforded, after the usual workup and crystallization from acetone/isooctane solution, colorless needles of the monoacetate **16** (180 mg, 83% theoretical): mp 150–151 °C; IR ($CHCl_3$) 3420, 2930, 2870, 1715, 1455, 1437, 1365, 1245, 1160, 1120, 960, 910, 840 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.00 (3 H, s), 1.04 (3 H, s), 1.10 (3 H, s), 1.11 (3 H, s), 1.14 (3 H, s), 1.19 (3 H, s), 1.25 (3 H, s), 1.76 (3 H, s), 2.14 (3 H, s), 2.48 (1 H, m), 3.33 (1 H, dd, J = 15.3, 4.4 Hz), 4.98 (1 H, d, J = 6.5 Hz), 5.46 (1 H, br dd, J = 8.0, 4.0 Hz); mass spectrum (CI, isobutane), m/e (relative intensity) 519 (MH^+, 5), 501 (59), 483 (63), 459 (41), 441 (90), 423 (100); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 170.25 (s), 143.11 (s), 121.39 (d), 82.05 (s), 79.18 (d), 77.26 (s), 76.84 (d), 72.32 (s), 57.61 (d), 56.02 (d), 52.78 (d), 48.89 (d), 42.60 (s), 39.24 (t), 37.24 (t), 35.44 (s), 35.05 (t), 33.70 (t), 31.67 (q), 30.00 (q), 30.00 (q), 29.47 (q), 29.06 (q), 26.87 (t), 26.54 (t), 25.55 (q), 25.00 (t), 24.77 (t), 23.00 (t), 21.48 (q), 21.21 (q), 12.88 (q).

Treatment of compound 1 (or **16**) (150 mg) with Ac_2O/pyridine solution (1 mL), at room temperature for 10 days, afforded after the usual workup the diacetate derivative **18** (175 mg, 99% theoretical): an oil; IR ($CHCl_3$) 2450, 2920, 2860, 1720, 1710, 1440, 1365, 1250, 1160, 1073, 1040, 1020, 962, 905 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.00 (3 H, s), 1.03 (3 H, s), 1.07 (3 H, s), 1.11 (3 H, s), 1.15 (3 H, s), 1.20 (3 H, s), 1.50 (3 H, s), 1.76 (3 H, br s), 1.96 (3 H, s), 2.16 (3 H, s), 2.49 (1 H, br d, J = 12.5 Hz), 3.36 (1 H, dd, J = 11.8, 4.4 Hz), 4.98 (1 H, d, J = 6.4 Hz), 5.49 (1 H, br dd, J = 8.2, 4.7 Hz); mass spectrum (CI, isobutane), m/e (relative intensity) 543 (MH^+ – 18, 5), 501 (13), 483 (71), 441 (62), 423 (100); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 170.61 (s), 170.25 (s), 143.23 (s), 121.39 (d), 93.38 (s), 79.24 (d), 77.29 (s), 76.87 (d), 72.29 (s), 57.55 (d), 56.08 (d) 52.96 (d), 45.03 (d), 42.66 (s), 39.30 (t), 35.65 (t), 35.44 (s), 35.11 (t), 33.76 (t), 31.70 (q), 30.02 (q), 30.02 (q), 29.60 (q), 29.09 (q), 26.90 (t), 26.60 (t), 24.63 (t), 23.85 (t), 23.01 (t), 22.71 (q), 21.51 (q), 21.24 (q), 20.94 (q), 12.91 (q).

Basic Hydrolysis of Compound 18. Compound **18** (50 mg) was dissolved in MeOH (6 mL) at 0 °C, and a solution of 2% KOH in MeOH (4 mL) was added. After 5 h the solution was neutralized (HOAc) and the solvent removed under vacuum. Chromatography on a silica gel column gave sipholenol-A (**1**, 31 mg, 73% theoretical) identical in all respects to the authentic material.

Acetylation of Sipholenol-B (5) with Acetic Anhydride in Pyridine. Treatment of sipholenol-B (**5**, 100 mg) with Ac_2O/pyridine solution (1 mL), at room temperature overnight, afforded, after the usual workup, a single oily product (**17**) (105 mg, 98% theoretical); IR ($CHCl_3$) 3590, 3440, 2930, 2850, 1720, 1440, 1360, 1245, 1155, 1135, 1070, 1045, 1015, 995, 980, 955, 905, 882 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.82 (3 H, s), 1.02 (3 H, s), 1.09 (3 H, s), 1.15 (3 H, s), 1.17 (3 H, s), 1.18 (3 H, s), 1.24 (3 H, s), 1.77 (3 H, br s), 2.14 (3 H, s), 2.50 (1 H, m), 3.50 (1 H, dd, J = 11.5, 4.5 Hz), 5.01 (1 H, d, J = 6.2 Hz), 5.54 (1 H, dd, J = 10.0, 4.5 Hz); mass spectrum (CI, isobutane), m/e (relative intensity) 519 (MH^+, 10), 501 (70), 483 (51), 459 (39), 441 (80), 423 (100); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 170.16 (s), 143.61 (s), 121.69 (d), 82.14 (s), 79.12 (d), 77.38 (s), 76.78 (d), 73.96 (s), 58.27 (d) 57.76 (d), 52.84 (d), 48.92 (d), 42.54 (s), 40.56 (t), 37.36 (t), 35.83 (t), 35.50 (s), 33.13 (t), 31.73 (q), 29.99 (q), 29.45 (q), 28.88 (q), 28.70 (t), 27.14 (t), 25.55 (q), 24.95 (t), 24.78 (t), 23.79 (q), 23.13 (t), 21.54 (q), 21.12 (q), 12.79 (q).

Treatment of compound **17** (10 mg) with Ac_2O/pyridine solution (0.4 mL) at 50 °C for 4 days, afforded, after the usual workup and chromatography on silica gel (eluted with increasing percent of $CHCl_3$ in petroleum ether), a single product, the diacetate **19** (8 mg, 68% theoretical): an oil; IR ($CHCl_3$) 3460, 2920, 2870, 1720, 1710, 1445, 1365, 1255, 1155, 1070, 1040, 1025, 960, 905 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.82 (3 H, s), 1.02 (3 H, s), 1.06 (3 H, s), 1.15 (3 H, s), 1.18 (3 H, s), 1.19 (3 H, s), 1.48 (3 H, s), 1.76 (3 H, s), 1.96 (3 H, s), 2.15 (3 H, s), 2.47 (1 H, br d, J = 12.5 Hz), 3.45 (1 H, dd, J = 10.5, 4.6 Hz), 4.97 (1 H, d, J = 6.5 Hz), 5.51 (1 H, br dd, J = 9.4, 4.1 Hz), mass spectrum (EI, 10 eV), m/e (relative intensity) 517 (M^+ – 43, 1), 501 (4), 483 (7), 423 (5), 265 (15), 222 (10), 216 (10), 206 (26), 191 (16), 188 (19), 179 (21), 148 (37), 122 (65), 84 (100).

Acetylation of Compound 2 with Acetic Anhydride. A few drops of Ac_2O were added to a solution of **2** (190 mg) in pyridine (2 mL), and the reaction mixture was kept at room temperature for 10 days. The pyridine was then evaporated in vacuo and the residue chromatographed on a Sephadex LH-20 column with $CHCl_3$/petroleum ether (65:35) as an eluant to yield compound **20**: 186 mg (90% theoretical); IR ($CHCl_3$) 3460, 2940, 2870, 1710, 1700, 1455, 1432, 1365, 1270, 1245, 1165, 1080, 1035, 1017, 940, 910 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.01 (3 H, s), 1.06 (3 H, s), 1.09 (3 H, s), 1.15 (3 H, s), 1.26 (3 H, s), 1.31 (3 H, s), 1.49 (3 H, s), 1.75 (3 H, br s), 1.95 (3 H, s), 2.48 (1 H, br d, J = 12.5 Hz), 2.92 (1 H, dd, J = 12.0, 3.7 Hz), 3.22 (1 H, ddd, J = 12.9, 11.0, 2.5 Hz), 5.49 (1 H, br dd, J = 8.5, 4.8 Hz); mass spectrum (EI, 15 eV), m/e (relative intensity) 456 (M^+ – AcOH, 12), 438 (31), 410 (3), 398 (4), 216 (34), 202 (20), 187 (37), 122 (100); ^{13}C NMR (22.63 MHz, $CDCl_3$) δ 218.0 (s), 170.5 (s), 143.1 (s), 121.5 (d), 93.3 (s), 82.4 (s), 81.2 (d), 72.2 (s), 57.5 (d), 55.7 (d), 52.9 (d), 44.8 (d), 42.0 (s), 39.6 (t), 39.2 (t), 35.7 (t), 35.4 (s), 35.0 (t), 33.9 (t), 31.7 (q), 30.0 (q), 30.0 (q), 29.6 (t), 26.7 (t), 26.6 (q), 26.6 (q), 24.6 (t), 23.9 (t), 22.7 (q), 20.9 (q), 20.5 (q), 12.2 (q).

Acetylation of Sipholenone-B (3). Sipholenone-B (**3**, 20 mg) was kept for 10 days in a mixture of Ac_2O (2 drops) and pyridine (4 drops) at room temperature. The usual workup afforded a single product, the 19-acetate **3a** (21 mg, 97% theoretical): an oil; IR ($CHCl_3$) 3500, 2920, 2875, 1725, 1700, 1380, 1365, 1250, 1210, 1080, 1025, 900 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.02 (3 H, s), 1.17 (3 H, s), 1.26 (3 H, s), 1.27 (3 H, s), 1.28 (3 H, s), 1.31 (3 H, s), 1.36 (3 H, s), 1.52 (3 H, s), 1.97 (3 H, s), 2.92 (1 H, dd, J = 12.0, 4.3 Hz), 2.94 (1 H, t, J = 7.5 Hz), 3.22 (1 H, ddd, J = 12.9, 11.0, 2.5 Hz); mass spectrum (EI, 10 eV), m/e (relative intensity) 473 (M^+ – AcO, 6), 455 (21), 397 (26), 395 (14), 378 (11), 374 (16), 356 (18), 330 (24), 299 (11), 292 (3), 291 (4), 273 (12), 270 (18), 256 (23), 228 (19), 219 (25), 204 (33), 161 (44), 150 (100).

Treatment of Compound 18 with Thionyl Chloride. A cold solution of a few drops of $SOCl_2$ in pyridine (1 mL) was added to a cold solution (0 °C) of **18** (80 mg) in pyridine (2 mL), and the reaction mixture was kept at 0 °C for 2 h. The pyridine was then evaporated in vacuo and the residue chromatographed on a short silica gel column with $CHCl_3$ as eluant to yield compound **21**: 72 mg (93% theoretical); an oil; IR ($CHCl_3$) 2915, 2860, 1720, 1460, 1440, 1370, 1250, 1150, 1100, 1050, 1014 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.98 (3 H, s), 1.01 (3 H, s), 1.07 (3 H, s), 1.17 (3 H, s), 1.22 (3 H, s), 1.51 (3 H, s), 1.56 (3 H, s), 1.75 (3 H, br s), 1.96 (3 H, s), 2.11 (3 H, s), 2.48 (1 H, br d, J = 12.5 Hz), 3.58 (1 H, dd, J = 11.7, 4.1 Hz), 4.98 (1 H, d, J = 6.2 Hz), 5.50 (1 H, br dd, J = 9.0, 5.0 Hz); mass spectrum (EI, 12 eV), m/e (relative intensity) 482 (M^+ – AcOH, 3.1) 422 (3), 407 (2), 341 (3), 338 (5), 295 (4), 279 (6), 267 (5), 229 (9), 219 (13), 213 (18), 203 (38), 201 (25), 189 (19), 128 (84), 122 (100); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 170.56 (s), 170.29 (s), 143.19 (s), 138.16 (s), 126.00 (s), 121.48 (d), 93.42 (s), 79.27 (d), 77.45 (s), 75.32 (d), 57.68 (d), 52.98 (d), 44.92 (d), 42.92 (s), 35.72 (t), 35.54 (s), 32.81 (t), 32.10 (t), 31.67 (q), 30.65 (t), 30.03 (q), 29.88 (t), 29.57 (q), 29.02 (q), 27.35 (t), 24.47 (t), 23.86 (t), 23.61 (t), 22.70 (q), 21.86 (q), 21.13 (q), 20.95 (q), 19.41 (q), 17.90 (q).

Treatment of Compound 19 with Thionyl Chloride. Compound **19** (8 mg) was treated with $SOCl_2$ as described for **18**. The residue was chromatographed on a short 2% $AgNO_3$-impregnated silica gel column and eluted with Et_2O. The less polar product (2 mg, 30% theoretical) was found to be identical in all respects with compound **21**. More polar product, compound **22** (2 mg, 30% theoretical): an oil; IR ($CHCl_3$) 2915, 2860, 1720, 1460, 1250, 1160, 1070, 1015 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.70 (3 H, s), 1.01 (3 H, s), 1.07 (3 H, s), 1.16 (3 H, s), 1.18 (3 H, s), 1.49 (3 H, s), 1.75 (3 H, br s), 1.95 (3 H, s), 2.16 (3 H, s), 3.54 (1 H, dd, J = 5.0, 11.4 Hz), 4.55 (1 H, s), 4.83 (1 H, s), 4.96 (1 H, d, J = 6.4 Hz), 5.50 (1 H, br dd, J = 9.0, 5.0 Hz); mass spectrum (EI, 12 eV), m/e (relative intensity) 452 (M^+, 1), 482 (4), 421 (2), 339 (4), 205 (8), 188 (7), 161 (9), 147 (17), 122 (53), 83 (100).

Transformation of Sipholenol-A (1) to Compound 23. To a cold solution of sipholenol-A (**1**, 350 mg) in CH_2Cl_2 (40 mL) was added a solution of *m*-chloroperbenzoic acid (180 mg) in CH_2Cl_2 (10 mL). After 3 h at 0 °C, a solution of 10% aqueous Na_2CO_3 (20 mL) was added and the heterogeneous solution stirred for 20 min. The two phases were separated and the CH_2Cl_2 phase washed with water (3 × 5 mL) and dried over anhydrous $MgSO_4$.

Evaporation of the solvent afforded a 95:5 mixture (365 mg, 98% theoretical) of the two isomeric epoxides. A $CHCl_3$ solution (50 mL) of this mixture (365 mg) was treated with *p*-TsOH acid (3 mg) at room temperature for 18 h and worked up as described above. The reaction mixture (350 mg) was chromatographed on a silica gel H column eluted with EtOAc to yield compound **23** (294 mg, 82% theoretical): amorphous material ($CHCl_3$); mp 181–183 °C; IR ($CHCl_3$) 3580, 3390, 2920, 2870, 1460, 1375, 1365, 1160, 1080, 1045, 910 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.82 (3 H, s), 0.97 (3 H, s), 1.08 (3 H, s), 1.12 (6 H, s), 1.19 (3 H, s), 1.25 (3 H, s), 3.49 (1 H, dd, J = 10.9, 4.0 Hz), 3.79 (1 H, d, J = 6.5 Hz), 4.42 (1 H, br t), J = 4.6 Hz), 4.82 (1 H, br s), 5.19 (1 H, br s); mass spectrum (CI, isobutane), m/e (relative intensity) 475 ($MH^+ - H_2O$, 6), 457 (37), 439 (100), 421 (45); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 152.21 (s), 113.04 (t), 81.85 (s), 77.93 (s), 77.09 (d), 76.56 (d), 72.72 (s), 72.21 (d), 55.33 (d), 51.36 (d), 46.69 (d), 42.89 (s), 39.66 (t), 39.25 (t), 36.98 (s), 34.22 (t), 32.58 (d), 32.58 (t), 32.08 (t), 30.38 (q), 29.25 (q), 26.79 (t), 25.91 (t), 25.66 (q), 25.40 (t), 25.40 (t), 24.95 (q), 23.33 (q), 2149 (q), 13.17 (q).

DDQ Oxidation of Compound 23. A solution of compound **23** (170 mg) and DDQ (100 mg) in 1:1 $CHCl_3$/toluene solution (20 mL) was kept at room temperature, in the dark, for 5 days, until all the starting material disappeared. The solvent was evaporated in vacuo and the crude reaction mixture chromatographed on silica gel H with $CHCl_3$/EtOAc (1:1) as the eluant to yield a single product (**24**) (150 mg, 89% theoretical); amorphous ($CHCl_3$); mp 142–143.5 °C; IR ($CHCl_3$) 3400, 2920, 2870, 1720, 1670, 1600, 1375, 1250, 1210, 1165, 1085, 1045, 960, 910 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.97 (3 H, s), 0.98 (6 H, s), 1.13 (6 H, s), 1.26 (3 H, s), 1.33 (3 H, s), 3.50 (1 H, dd, J = 5.3, 11.7 Hz), 3.81 (1 H, d, J = 6.7 Hz), 5.23 (1 H, d, J = 2.0 Hz), 6.14 (1 H, d, J = 2.0 Hz); mass spectrum (CI, isobutane), m/e (relative intensity) 491 (MH^+, 1), 473 (35), 455 (100), 437 (93), 419 (19); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 202.59 (s), 147.59 (s), 125.84 (t), 82.19 (s), 78.03 (s), 76.80 (d), 76.44 (d), 72.10 (s), 56.88 (d), 55.11 (d) 51.16 (d), 48.76 (d), 42.65 (s), 42.14 (t), 39.09 (t), 36.99 (s), 36.84 (t), 34.11 (q), 33.75 (t), 32.15 (q), 29.95 (q), 28.99 (q), 28.42 (t), 26.56 (t), 26.26 (t), 25.54 (q), 25.21 (t), 24.73 (t), 21.35 (q), 12.90 (q).

Ozonolysis of Sipholenol-C (6). A cooled solution (−78 °C) of **6** (25 mg) in CH_2Cl_2 (2 mL) was titrated with a saturated blue solution of O_3 in CH_2Cl_2 (ca. 0.04 M, 5 mL). After 5 min at −78 °C, the mixture was allowed to warm up to room temperature and the solvent was removed under vacuo. The residual oil was taken in acetone (5 mL) and oxidized with a few drops of a Jones reagent. Following the usual workup, the residue (25 mg) was chromatographed on a silica gel column, eluted with increasing percent of EtOAc in $CHCl_3$ fractions of 10 mL each. Fraction 3 eluted with 20% EtOAc in $CHCl_3$ gave pure **27** (10 mg, 68% theoretically): an oil; IR ($CHCl_3$) 2920, 2850, 1770, 1710, 1460, 1380, 1285, 1170, 1125, 1095, 1068, 905 cm^{-1}; mass spectrum (EI, 12 eV), m/e (relative intensity) 280 (M^+, 3), 265 ($M^+ - CH_3$, 10), 252 ($M^+ - CO$, 14), 238 ($M^+ - CH_2CO$, 100), 222 (4), 197 (33), 195 (10), 194 ($M^+ - CO - C_3H_6O$, 23), 179 (194 − CH_3, 28), 166 (28), 151 (12), 138 (22), 129 (23), 121 (21). For ^1H NMR data, see Scheme IV. Fraction 6 eluted with the same solvent system gave **28**: an oil; mass spectrum, m/e 206 ($M^+ - H_2O$); IR ($CHCl_3$) 3450, 2970, 1705, 1240, 1175 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.14 (1 H, m), 1.47 (3 H, s), 1.28 (3 H, d, J = 7.5 Hz), 1.15 (3 H, s), 1.06 (3 H, s).

Jones Oxidation of Compound 26. Jones oxidation of sipholenol-E monoacetate (**26**, 3 mg) in the same manner described above for **2** gave the α,β-unsaturated ketone **25** (2 mg, 70% theoretical) identical in all respects with the authentic sample (see above); an oil; IR ($CHCl_3$) 3590, 3450, 2925, 2870, 1720, 1660, 1645, 1440, 1360, 1245, 1070, 1035, 960, 905 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.75 (3 H, s), 0.98 (3 H, s), 1.03 (3 H, s), 1.16 (3 H, s), 1.18 (3 H, s), 1.20 (3 H, s), 1.25 (3 H, s), 1.90 (3 H, s), 2.13 (3 H, s), 2.31 (1 H, dd, J = 12.5, 7.0 Hz), 2.37 (1 H, dd, J = 12.5, 3.8 Hz), 2.70 (1 H, br d, J = 5.0 Hz), 3.39 (1 H, dd, J = 11.5, 4.3 Hz), 4.98 (1 H, d, J = 6.6 Hz); ^{13}C NMR (75.46 MHz, $CDCl_3$) δ 199.75 (s), 170.22 (s), 161.98 (s), 132.74 (s), 79.15 (d), 77.26 (s), 76.61 (d), 72.17 (s), 71.33 (s), 56.08 (d), 45.72 (d), 45.48 (d), 43.08 (s), 40.41 (t), 39.51 (t), 38.17 (t), 36.46 (t), 35.92 (t), 35.59 (s), 34.24 (t), 30.67 (q), 30.52 (t), 29.02 (q), 28.52 (q), 26.54 (t), 24.23 (t), 23.09 (q), 22.67 (q), 21.48 (q), 21.21 (q), 13.09 (q), 11.71 (q). For mass spectral data, see Table III.

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Ant-Repellent Triterpenoids from *Cordia alliodora*

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Six triterpenoids have been isolated from leaves of the tropical tree *Cordia alliodora* (Boraginaceae) and assigned structures on the basis of spectral and crystallographic data and chemical interconversions. All six compounds, 3α-hydroxyolean-12-en-27-oic acid and five oxidized derivatives, were found to be significantly ant repellent in a bioassay that measures the feeding preferences of the leafcutter ant *Atta cephalotes*.

The leafcutter ants (Hymenoptera, Formicidae, Attini) are classed as agricultural pests throughout the tropical Americas, both because of the massive amount of leaf material they harvest and their special fondness for agriculturally important plant species. Colonies whose foraging is restricted to areas of native forest encounter a great variety of potential host plants, but while the leafcutter ants are considered polyphagous, they are nonetheless quite specific in their preference for some plant species and dislike of others.[1] From native plant species that escape leafcutter attack, we have reported the isolation of the ant-repellent sesquiterpenoids lasidiol angelate[2,3] and caryophyllene epoxide.[3] In continuation of our

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